REMARKS

The presently claimed invention concerns polypeptides that are at least 80% identical to SEQ ID NO:9, an *M. incognita* PEAMT1-like enzyme.

Claims 9-11 have been amended to specify that the claimed polypeptides have methyltransferase activity.

Applicants appreciate the notification that claim 12 is allowed.

Rejections under 35 U.S.C. §112, first paragraph (written description)

The Examiner rejected claims 9-11 as allegedly failing to meet the written description requirement. The Examiner argued that the specification provides only a single representative species of the claimed invention and that the specification fails to provide both "identifying structural characteristics or properties" and "structure to function/activity relationships"

The present claims have been amended to specify that the claimed polypeptides hade methyltransferase activity. Thus, the present claims define the claimed polypeptides by both structure (percent identity to a specified polypeptide sequence) and function (methyltransferase activity). As explained in greater detail below, these claims are supported by written description that meets the requirements of 35 U.S.C. §112, first paragraph.

SEQ ID NO:9 is the amino acid sequence of an *M. incognita* protein that is related to proteins of the plant phosphoethanolamine n-methyltransferase gene family and to similar proteins found in C. elegans. As explained in the specification, plant methyltransferases from spinach and *Arabidopsis* have been cloned. These plant methyltransferases have been shown to act on phosphoethanolamine and are predicted to encode soluble proteins of approximately 55kDa that have two domains containing separate SAM binding sites. Each domain contains motifs - termed Motif I, Post-I, Motif II, and Motif III – that are conserved among SAM-dependent methyltransferases.

SEQ ID NO:9 is similar to the portion of spinach phosphoethanolamine n-methyltransferase that catalyzes the methylation of pEA to pMME, the first of two methylation reactions carried out by the spinach enzyme. Thus, SEQ ID NO:9 is referred to as a PEAMT1-like enzyme.

Applicants have disclosed several PEAMT1-like enzymes

The Examiner stated that the specification discloses only a single phosphoethanolamine n-methyltransferase, i.e., SEQ ID NO:9. Applicants disagree.

The present specification discloses three PEAMT1-like enzymes from parasitic nematodes in addition to SEQ ID NO:9:

A. suum PEAMT1-like enzyme (SEQ ID NO:7; Figure 1);

H. contortus PEAMT1-like enzyme (SEQ ID NO:8; Figure 2); and

S. stercoralis PEAMT1-like enzyme (SEQ ID NO:10; Figure 4).

As explained in the specification at pages 8-9, *A. suum* is the large roundworm of pigs and is closely related to *Ascaris lumbricoides*, a major human pathogen. *H. contortus* is a parasite of ruminants (sheep, goats, cattle and other wild ruminants) leading to emaciation, anemia and in certain cases death. *S. stercoralis* is a nematode parasite that infects humans, primates, and dogs. Thus, Applicants have disclosed the amino acid sequence of PEAMT1-like enzymes from several diverse parasitic nematode species. In addition to the parasitic nematode enzymes described above, Applicants have identified two splice variants of a *C. elegans* gene encoding a PEAMT1-like enzyme. The polypeptides encoded by these two splice variants are shown in SEQ ID NO:19 and 20.

In view of the forgoing it is clear that Applicants have disclosed not just one, but several nematode PEAMT1-like enzymes.

Applicants have identified conserved motifs and conserved regions in PEAMT1-like enzymes

The Examiner stated that the specification failed to identify structural characteristics of the claimed polypeptides and failed to disclose "any particular function/activity relationship.

Applicants disagree. In fact, Applicants have provided sequence alignments and identified conserved domains among the disclosed proteins.

As explained in the specification, S-adenosylmethionine (SAM)-dependent methyltransferase proteins contain four conserved motifs which define the SAM-binding site (Kagan & Clarke (1994) *Arch Biochem Biophys.* 310:417-427). The four domains are commonly referred to as Motif I, Post I, Motif II, and Motif III. In the present specification Applicants provided a table (Table 3) showing the locations of the these conserved motifs in the four disclosed parasitic nematode PAMT1-like enzymes and in the two *C. elegans* PEAMT1-like enzyme splice variants. This table, which is presented on page 33 of the specification, is reproduced below for the Examiner's convenience.

Nematode	Motif I	Post I	Motif II	Motif III
A. suum	56-63	76-80	114-120	143-152
H. contortus	56-63	76-80	114-120	143-152
M. incognita	64-71	84-88	122-128	151-160
S. stercoralis	56-63	76-80	118-124	147-156
C. elegans $_a$	70-77	90-94	128-134	157-166
C. elegans $_b$	79-86	99-103	137-143	166-175

The identification of the location of the conserved motifs amounts to a disclosure of structural characteristics of the claimed polypeptides.

Figure 7 of the present application, which is reproduced below for the Examiner's convenience, is an alignment of the sequences of *A. summ, H. contortus, M. incognita* and *S. stercoralis* PEAMT1-like enzymes (SEQ ID NO: 7, 8, 9 and 10) and *C. elegans* PEAMT1-like polypeptides (SEQ ID NO: 19 and 20). This alignment allows one to readily identify conserved regions among the disclosed PEAMT1-like enzymes and provide structure/function relationships for nematode PEAMT1-like enzymes.

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C_elegans_a   ...MSTDQQ......SSVEDQTVAMVNVRRANPKSPWDKYSDKPDTNSMMLNHSAEELES: 51
C_elegans_b   MDRYSPYDKTVPLIPCTAYILQKAMVNVRRANPKSPWDKYSDKPDTNSMMLNHSAEELES: 60
H_contortus   .....................MTAEVRRDSPKTPWDKYSDKPDTNSMMLNQTAQDLEA: 37
A_summ        .....................MTEAIRRSSPKNPWSKPSHRCDNTVMMLNKSADEPEA: 37
M_incognita   ..............MRMRLEHEDTDMDWRQIYHSPWNKPSDRADNTSMLLNADADKPEA: 45
S_stercoralis .....................MEGENDRQNPLEYWRQPGNIANINGMMLNANASLIEK: 37

C_elegans_a   SDRADILASLPLLHNKDVVDIGAGIGRPTTVLAETARWVLSTDPIDSPIKKNQERNAHLG:111
C_elegans_b   SDRADILASLPLLHNKDVVDIGAGIGRPTTVLAETARWVLSTDPIDSPIKKNQERNAHLG:120
H_contortus   SDRADILSSLPHLTNKDVVDIGAGIGRPTTVLAETARWVLSTDPIESPIEKNQERNAHMG: 97
A_summ        DDRADIISSLPDLHGKDIVDIGAGIGRPTTIFAHDARHVLSCDPIESPMAKNKERNAHPS: 97
M_incognita   LDRAEIIGMLPSPKNKPVVDIGAGIGRPTTEPAKKAREVVSTDPVASPIEKNRETNIAPN:105
S_stercoralis NDRHDVCLLLPDLKGKTVLDAGAGIGRPTAELAERAEKVYASDPISEYVTKLQELSAEAL: 97

C_elegans_a   N....INYQVGDAVGLKMESNSVDLVFTNWLMMYLSDEETVEPIFNCMRWLRSHGIVHLR:167
C_elegans_b   N....INYQVGDAVGLKMESNSVDLVFTNWLMMYLSDEETVEPIFNCMRWLRSHGIVHLR:176
H_contortus   N....ISYQIGDAVHLQMDEKSVDLVFTNWLMMYLSDREVIEPLLNAMRWLRADGYIHLR:153
A_summ        N....ISYQVGDAVHLQLDPNSVDLVFTNWLMMYLSDDEVIRPLLNALRWLRPNGYLHLR:153
M_incognita   N....IEWRVGDAVRLDFEEGSIDIVFTNWLLMYLVDEEVVQPLINAIKWLRPGGYLHLR:161
S_stercoralis KNGKIIDVTVADATCLSYPENSYFLVFTNWLFMYFNNTECVRPTVNALKWLEEGGYFKLR:157

C_elegans_a   ESCSEPSTGRS...KAKSMHDTANANPTHYRFSSLYINLLRAIRYRDVDNKLWRFNVQWS:224
C_elegans_b   ESCSEPSTGRS...KAKSMHDTANANPTHYRFSSLYINLLRAIRYRDVDNKLWRFNVQWS:233
H_contortus   ESCSEPSTGRL...KTATMHSAVDANPTHYRFSSLYIKLLRAIRYGDSDGKMWKFDVQWS:210
A_summ        ESCSQPSTAR....VGGTMHNSTEINPTSYRLSSEYIKLLRNIRYRELDGTLFRFEVHWA:209
M_incognita   ESCSEPSSKKS...NNSLHSNSDSINPTKYRFSSAYIQLLKSINFKSGDGTVWGFKIHWA:218
S_stercoralis ESCSEPSTRRVGNRNETSLHAAVQSNPTEYRFSSVYLKLIEAARYVDSNNQKWKFEIEIC:217

C_elegans_a   CSVPTYIKRSNNWRQVHWLAEKVPAEDGAKGTSFNELVELIKNTWQNEQEAWDAKLD...:281
C_elegans_b   CSVPTYIKRSNNWRQVHWLAEKVPAEDGAKGTSFNELVELIKNTWQNEQEAWDAKLD...:290
H_contortus   CSVPTYIRRCNNWRQVHWLTKKVPAVGDEE.TSVDDLLNLFSQIWPAEQKTWDEKLD...:266
A_summ        CSVPTYIVVQNNWRQVHWLTQKVRCNDDAI.MSIEHLLGHFSTLWKVEQQKWDRYLD...:265
M_incognita   SSVNVYIQKNANWRQVHWLVSKVPKKE....KFMPNLGTLLGEKWPEEQKEWDNKLDLAL:274
S_stercoralis GSIPTYILNGNTWRQVQLIAKKVKADDNDVVLSQDELKNLMTNDWIMEQKKTDSIVD...:274

C_elegans_a   DEKYVWTDKVPSSALT.....SLPSNSTPFLYTPRTVSPYCHINAHTLAETFNAN.VWNT:335
C_elegans_b   DEKYVWTDKVPSSALT.....SLPSNSTPFLYTPRTVSPYCHINAHTLAETFNAN.VWNT:344
H_contortus   NEKYSWTDKIPSNAIDDE...VVPKNSTAYVFTPRQRSPFLHVNSHLLAEKFTCN.VWNV:322
A_summ        NESYCWTDEVFGYALMKE...TIESMPAVLAYNPRKLAYHLHINAHRISEMLHCNVVWNV:322
M_incognita   NENQNITSTLASYLLSS....GIGTNSVILVFDLRNSENQPSINVHTLANRLNSN.IWSV:329
S_stercoralis GRVQYFADKIFANELSNIDMTNTESISSIFVFQSSFNPWYKRIFPPSLASNKYCH.VWTN:333

C_elegans_a   EIIPEYYRTSLTKSNNLKDQRVRFGWN.QSLTDSVTYWQQKDALFDVFVATEFLSTVDDE:394
C_elegans_b   EIIPEYYRTSLTKSNNLKDQRVRFGWN.QSLTDSVTYWQQKDALFDVFVATEFLSTVDDE:403
H_contortus   ETKEYLYRTSLTKANNQKDQRVRFGWN.ESLSSPIDYWNQRDASFDCMVATELLATCDDE:381
A_summ        EINEFFYRTSLTKANRLKDQRVRFGWN.ATLESSLNYWKERGALFDIFIATEFFTDLDES:381
M_incognita   SLNPFCFRHSLTLANNNQDRRIRHSWH.EDIESAPHFLGEQISGKEKNISRLFDVIIGIG:388
S_stercoralis EGNRELFRCSLTSANEERNIGMFFTYSKDNVFNALDYVKKRNFLLNSFLAIDYLNNHEVN:393

C_elegans_a   TIRQLPNVMSDGAKFITLEP..VDEVNEAEMKQRIQELGYTLKSFTDVTDQCIEAQEQYF:452
C_elegans_b   TIRQLPNVMSDGAKFITLEP..VDEVNEAEMKQRIQELGYTLKSFTDVTDQCIEAQEQYF:461
H_contortus   SVKSIASIMKPEAKVVLLEP..VSGIDETSVRQRMTTCGPKNITIVDVTQESLNAEVSPI:439
A_summ        TIDKLSVVLKADAPLILLEP..FDESAYDEKYIMKLLSRYQQISIEDITEMCTEAIHKYL:439
M_incognita   LLEKIKKMKDASEKVEKILGRYLLSIETGEGDDIRKERKNEDIVEYFPSELPTKQTIEPK:448
S_stercoralis FIESFNNIASQDAKILLLES..PSNEDE...KNLKLSKLNKQYTVKCVTENVHNEVKNVH:448

C_elegans_a   KDHEQLRDEKVIRKNWVLLELTH:475
C_elegans_b   KDHEQLRDEKVIRRNWVLLELTH:484
H_contortus   KDHN..LDVELSGCNYLLIKASL:460
A_summ        SERD..LENNIGTKVWKLIKAHM:460
M_incognita   ADNG..........FNQLD...:457
S_stercoralis QDEE..IVCDVTSKKWMLINVNH:469
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In view of the forgoing, it is Applicants position that the specification provides a written description of the claimed invention that meets the requirements of 35 U.S.C. §112, first paragraph, and Applicants request that these rejections be withdrawn.

Rejections under 35 U.S.C. §112, first paragraph (enablement)

The Examiner rejected claims 9-11 as allegedly not enabled. According to the Examiner, it would require undue experimentation to make and use polypeptides that are at least 80% identical to SEQ ID NO:9. The Examiner argued that the specification does not establish:

> (A) regions of the protein structure which may be modified without affecting ...phosphoethanolamine n-methyltransferase activity; the (B) the general tolerance of ...phosphoethanolamine n-methyltransferases to modification . . . (C) a rational and predictable scheme for modifying any amino acid residue ... with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

First, as noted above, Applicants have amended claims 9-11 to specify that the claimed polypeptide has methyltransferase activity.

Second, as explained above in a different context, the present specification provides considerable guidance for one skilled in the art wishing to make functional proteins having at least 80% identity to SEQ ID NO:9. For example, as noted above, Table 3 of the specification identifies 4 motifs in SEQ ID NO:9 that are believed to be important for methyltransferase activity. In addition, also as noted above, Figure 7 of the specification provides an alignment of the sequences of *A. summ, H. contortus, M. incognita* and *S. stercoralis* PEAMT1-like enzymes (SEQ ID NO: 7, 8, 9 and 10) and *C. elegans* PEAMT1-like polypeptides (SEQ ID NO: 19 and 20). This alignment allows one to readily identify conserved regions among the disclosed PEAMT1-like enzymes. Taken together, the identification of motifs and the alignment provide considerable guidance for one making functional proteins having at least 80% identity to SEQ ID NO:9.

In view of the forgoing, Applicants respectfully request that the these rejections under 35 U.S.C. §112, first paragraph be withdrawn.

It is believed that the claims are in condition for allowance. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

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